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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,306	02/14/2001	Uwe Wenzel	51202	2453

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EXAMINER

KHARE, DEVESH

ART UNIT PAPER NUMBER

1623

DATE MAILED: 02/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/782,306

Applicant(s)

WENZEL ET AL.

Examiner

Devesh Khare

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 5-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>2</u> . | 6) <input type="checkbox"/> Other: _____ |

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Status of the Restriction

The response to restriction requirement received on 12/10/02 has been entered.

Applicants' election of Group I (claims 1 and 2) with traverse in Paper No. 4 is acknowledged. In view of the similarity in the mode of action and effects of the compositions between the compositions claimed in claims 1 and 2 and a method for inhibiting COX-2 biosynthesis in claims 3 and 4 with the said composition, the restriction requirement of Group II (claims 3 and 4) is withdrawn. Applicant's arguments are convincing.

Claims 5-12 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-12 are currently pending in this application. An action on the merits of claims 1-4 is contained herein below.

Minor objections

Claim 1 is objected to because of the following informalities:

Claim 1, lines 19-20; misspell the words "rutinoside" and "apiosylglucoside".*

Claim 1, line 15 is objected to for failing to end in a comma separating the phrase "R⁵, R⁶".

Claim 1, line 20 is objected to for failing to end in a comma separating the phrase "R² and R³".

Claim 1, line 33, misspell the word "Phenyl-ring".*

*-denotes that error can also be found in the specification and abstract.

Appropriate correction is required.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation "R⁵, R⁶, R⁷, R⁸ represent independently of each other Hydrogen, Hydroxy or Methoxy", and the claim also recites "a sugar substituent like glucoside, rutinoside...." which is the narrower statement of the range/limitation.

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In claim 1, line 19, the Markush group "manno gluco pyranosyl" is vague and indefinite in that the chemical nomenclature is not seen to be conventional and is inconsistent with a sugar substituent. The same error can also be found in the specification and abstract.

2. Claims 3 and 4 are confusing. Each method claim, which recites the phrase "to a patient in need of", is awkward and confusing. In all occurrences the current claim language renders the method claims wherein this recitation is set forth indefinite. The administration of the active agent should be clearly set forth before the term "comprising", the terms --- in a patient ---.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nair et al. (U.S. Patent 6,194,469, filed 06-1999) in view of Yoshikumi et al. (U.S. Patent 4,440,757).

The claims 1-4 are directed to a composition for inhibiting cyclooxygenase (COX) enzymes, which are broadly comprised of two components:

(1) a composition for inhibiting COX-2(cyclooxygenase-2) or Cox-2 and NF κ B(nuclear factor kappa B) biosynthesis, which comprises a bioflavonoid represented by the

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formula I and II where a sugar selected from glucoside, rutinoside or apiosylglucoside is attached to C-7 position in said bioflavonoid; and

(2) a method for inhibiting COX-2 or NF κ B or Cox-2 and NF κ B biosynthesis by administering to a patient, a therapeutically effective amount of compound of claim 1 (formula I) or claim 2 (formula II).

Nair et al. teach a composition and a method for inhibiting cyclooxygenase enzymes using a mixture of anthocyanins, bioflavonoids and phenolics (see abstract). Nair et al. disclosed the importance of plant-derived compounds as anti-inflammatory agents by inhibiting prostaglandin synthesis or cyclooxygenase (COX) enzymes (see col. 1, lines 33-35 and col. 2, lines 43-46). In column 6, lines 8-18, a composition of the mixtures of anthocyanins, bioflavonoids and phenolics is taught. In column 9, Example 5, a method to inhibit COX-2 activity by flavonoids and isoflavonoids is disclosed (see col. 9, lines 45-60). Applicants use of formula I and II, where a glucoside is attached to C-7 position in a flavonoid for inhibiting COX-2 biosynthesis according to claim 3 and 4 is seen to be rendered obvious, see col. 11, lines 29-34 of Nair et al., wherein the inhibitory activity of C-7 glucosylated genistin isoflavonoid is disclosed.

While the Nair et al. compositions and method to inhibit COX-2 activity by flavonoids and isoflavonoids are closely analogous to applicant's, Nair et al's. compositions differ from applicant's compositions in that the most of flavonoids and isoflavonoids used for inhibition studies of COX-2 are glycosylated at C-3 position, except genistin, which is glucosylated at position C-7. However Nair et al. does provide motivation to use natural products for use as cyclooxygenase inhibitors and as anti-inflammatory agents (see col.

3, lines 17-19). Use of a known member of a class of materials in a process is not patentable if other members of the class were known to be useful for that purpose, even though results are better than expected.

Yoshikumi et al. teach a pharmaceutical composition for regulating prostaglandins (see abstract). On column 6, lines 8-18, a composition for use in regulating prostaglandins is disclosed, wherein a glycosylated derivative of aminobenzoic acid represented by formula (1) is an active ingredient. Yoshikumi et al. disclose the effect of an anti-inflammatory drug, indomethacin, which relates to cyclooxygenase in the regulation of prostaglandins in col. 10, lines 65-67. It is noted that Yoshikumi et al. does not provide specific disclosures regarding the use of a bioflavonoid in the inhibition of a cyclooxygenase.

Therefore, one of ordinary skill in the art would have found the applicants claimed composition of formula I and II and method a method for inhibiting COX-2 biosynthesis, to have been obvious at the time the invention was made having the above cited references before him. Since Nair et al. teach a composition and a method for inhibiting prostaglandin synthesis or cyclooxygenase (COX) enzymes using the plant-derived compounds as anti-inflammatory agents and Yoshikumi et al. teach a pharmaceutical composition for regulating prostaglandins, one skilled in the art would have a reasonable expectation for success in combining both references to accomplish a composition comprising formula I and II and a method for regulating prostaglandin by

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inhibiting COX-2(cyclooxygenase-2) or Cox-2 and NF κ B(nuclear factor kappa B) biosynthesis by using the said composition.

State of the Art References

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Watanabe et al. (U.S. Patent 5,650,433)- discloses a chondroprotective agent comprising a flavonoid compound.

Wierzbicki et al. (U.S. Patent 5,792,789)- discloses the bioflavonoid diosmetin and its use as medicament.

Kwak et al. (U.S. Patent 5,910,307)- discloses the plant extracts and their inhibition activity of COX-2 enzymes.

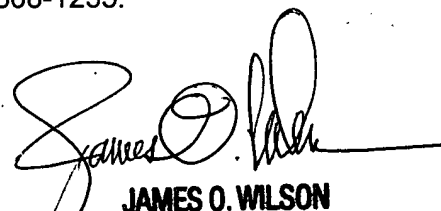
Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (703)605-

1199. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 703-308-4624. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,JD(3Y).
Art Unit 1623
January 29,2003


JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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